riboflavin transporter deficiency neuronopathy

Riboflavin transporter deficiency neuronopathy is a disorder that affects nerve cells (neurons). Affected individuals typically have hearing loss caused by nerve damage in the inner ear (sensorineural hearing loss) and signs of damage to other nerves.

In addition to nerves in the inner ear, riboflavin transporter deficiency neuronopathy involves nerves found in the part of the brain that is connected to the spinal cord (the brainstem), specifically in a region of the brainstem known as the pontobulbar region. Damage to these nerves causes paralysis of the muscles controlled by them, a condition called pontobulbar palsy. Nerves in the pontobulbar region help control several voluntary muscle activities, including breathing, speaking, and moving the limbs. As a result of pontobulbar palsy, people with riboflavin transporter deficiency neuronopathy can have breathing problems; slurred speech; and muscle weakness in the face, neck, shoulders, and limbs. Affected individuals can also have muscle stiffness (spasticity) and exaggerated reflexes.

The age at which riboflavin transporter deficiency neuronopathy begins varies from infancy to young adulthood. When the condition begins in infancy, the first symptom is often breathing problems caused by nerve damage, which can be life-threatening. When the condition begins in children or young adults, sensorineural hearing loss usually occurs first, followed by signs of pontobulbar palsy.

If not treated, the signs and symptoms of riboflavin transporter deficiency neuronopathy worsen over time. Severe breathing problems and respiratory infections are the usual cause of death in people with this condition. Without treatment, affected infants typically survive less than one year. However, those who develop the condition after age 4 often survive more than 10 years.

Riboflavin transporter deficiency neuronopathy encompasses two conditions that were once considered distinct disorders: Brown-Vialetto-Van Laere syndrome (BVVLS) and Fazio-Londe disease. The two conditions have similar signs and symptoms, but Fazio-Londe disease does not include sensorineural hearing loss. Because these two conditions share a genetic cause and have overlapping features, researchers determined that they are forms of a single disorder.

Frequency

Riboflavin transporter deficiency neuronopathy is a rare condition. Approximately 100 cases have been reported in the scientific literature.

Genetic Changes

Riboflavin transporter deficiency neuronopathy is caused by mutations in the *SLC52A2* or *SLC52A3* gene. These genes provide instructions for making related proteins called riboflavin transporters: RFVT2 is produced from the *SLC52A2* gene, and RFVT3 is produced from the *SLC52A3* gene. Both proteins move (transport) a vitamin called riboflavin (also called vitamin B_2) across the cell membrane. Riboflavin cannot be made by the body, so it must be obtained from the food a person eats. The RFVT3 protein is found at especially high levels in cells of the small intestine and is important for absorbing riboflavin during digestion so that the vitamin can be used in the body. The RFVT2 protein is found in cells of the brain and spinal cord and is important for ensuring that these tissues have enough riboflavin for proper functioning.

In the cells of the body, riboflavin is the core component of molecules called flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN). FAD and FMN are involved in many different chemical reactions and are required for a variety of cellular processes. One important role of these molecules is in the production of energy for cells. FAD and FMN are also involved in the breakdown (metabolism) of carbohydrates, fats, and proteins.

Mutations in the *SLC52A2* or *SLC52A3* gene lead to an abnormal riboflavin transporter protein with impaired ability to transport riboflavin. Consequently, there is a reduction of riboflavin available in the body. However, it is unclear how these changes lead to the nerve problems characteristic of riboflavin transporter deficiency neuronopathy.

Inheritance Pattern

Riboflavin transporter deficiency neuronopathy usually follows an autosomal recessive pattern of inheritance, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Brown-Vialetto-Van Laere syndrome
- BVVLS
- Fazio-Londe disease
- Fazio-Londe syndrome
- pontobulbar palsy with deafness
- progressive bulbar palsy with sensorineural deafness
- riboflavin transporter deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Brown-Vialetto-Van Laere syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796274/

Other Diagnosis and Management Resources

- GeneReview: Riboflavin Transporter Deficiency Neuronopathy
  https://www.ncbi.nlm.nih.gov/books/NBK299312

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Riboflavin
  https://medlineplus.gov/ency/article/002411.htm
- Encyclopedia: Sensorineural Deafness
  https://medlineplus.gov/ency/article/003291.htm
- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Neurologic Diseases
  https://medlineplus.gov/neurologicdiseases.html
- Health Topic: Neuromuscular Disorders
  https://medlineplus.gov/neuromusculardisorders.html

Genetic and Rare Diseases Information Center

- Riboflavin transporter deficiency
  https://rarediseases.info.nih.gov/diseases/9993/riboflavin-transporter-deficiency

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Motor Neuron Diseases Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Motor-neuron-diseases-Information-Page

Educational Resources

- BVVL International: About BVVL
  http://www.bvvlinternational.org/about-bvvl.html
- Disease InfoSearch: Brown-Vialetto-Van Laere Syndrome
  http://www.diseaseinfosearch.org/Brown-Vialetto-Van+Laere+Syndrome/978
- MalaCards: riboflavin transporter deficiency neuronopathy
  http://www.malacards.org/card/riboflavin_transporter_deficiency_neuronopathy
- Oregon State University Linus Pauling Institute: Riboflavin
  http://lpi.oregonstate.edu/mic/vitamins/riboflavin
- Orphanet: Riboflavin transporter deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=97229

Patient Support and Advocacy Resources

- BVVL International
  http://www.bvvlinternational.org/
- Facial Palsy UK
  http://www.facialpalsy.org.uk/causesanddiagnoses/brown-vialetto-van-laere-syndrome/

GeneReviews

- Riboflavin Transporter Deficiency Neuronopathy
  https://www.ncbi.nlm.nih.gov/books/NBK299312

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28brown-vialetto-van+laere+syndrome%5BTIAB%5D%29+OR+%28bvvls%5BTIAB%5D%29+OR+%28pontobulbar+palsy+with+deafness%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- BROWN-VIALETTO-VAN LAERE SYNDROME 1
  http://omim.org/entry/211530

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